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10/757,295	01/14/2004	Axel Riedel	01-1442	4516

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EXAMINER	
ROYDS, LESLIE A	
ART UNIT	**PAPER NUMBER**
1614	

NOTIFICATION DATE	DELIVERY MODE
06/05/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

USPTO.e-Office.rdg@boehringer-ingelheim.com

Office Action Summary	Application No.	Applicant(s)	
	10/757,295	RIEDEL ET AL.	
	Examiner	Art Unit	
	LESLIE A. ROYDS	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 March 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2 and 7-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2 and 7-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 2 and 7-18 are presented for examination.

Applicant's Amendment filed March 25, 2009 has been received and entered into the present application.

Claims 2 and 7-18 remain pending and under examination.

Applicant's arguments, filed March 25, 2009, have been fully considered. Rejections not reiterated from previous Office Actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set of rejections presently being applied to the instant application.

Claim Rejections - 35 USC § 112, First Paragraph, Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2 and 7-13 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of asthma, bronchitis, interstitial lung disease, insulin resistance, prediabetes, type 2 diabetes mellitus, metabolic syndrome, hypertension combined with hyperlipidemia or hypertension combined with atherosclerosis comprising the administration of telmisartan (or a salt thereof) with atorvastatin (or a salt thereof), does not reasonably provide enablement for the prevention of the same, for the reasons of record set forth at p.2-8 of the previous Office Action dated November 25, 2008, of which said reasons are herein incorporated by reference.

Response to Applicant's Arguments

Applicant traverses the instant rejection, stating that the Examiner states that metabolic syndrome is complex, but does not explain why there is any doubt as to the effectiveness of prevention using the

claimed method. Applicant again relies on the reasoning in *Ex parte Cho* to support his position that the instant embodiments directed to prevention are enabled. Applicant further alleges that the Examiner has not met her burden of providing any reasoning as to why prevention of the other conditions in the claims is also not enabled.

Applicant's traversal has been fully and carefully considered, but fails to be persuasive.

Firstly, the allegation that the Examiner has made the unsupported statement that metabolic syndrome is complex but provides no explanation as to the why there is any doubt as to the effectiveness of prevention using the claimed method is not a point well taken because it clearly does not appreciate the entirety of the rejection as it was set forth in the previous Office Action. Applicant is directed to p.2-8 of the Office Action dated November 26, 2008, which cites to literature by Grundy that supports the complexity of treating and managing, let alone preventing, the condition of metabolic syndrome. Furthermore, extensive rationale and reasoning was provided in conjunction with the Grundy reference to support the conclusion of a lack of enabling guidance, which Applicant is invited to reconsider. Accordingly, Applicant's remarks that the Examiner has not provided any reasoning to doubt the effectiveness of the preventive embodiments claimed are clearly erroneous and unpersuasive.

Secondly, Applicant persists in applying the reasoning of *Ex parte Cho* to the instant case. This is again, and will remain, unpersuasive. Applicant has failed to, at the very least, point out how the facts in a case decided regarding the enablement of prevention of two distinct and different therapeutic indications using two structurally, functionally and chemically distinct compounds are similar to the instant application. However, even if, *arguendo*, Applicant did provide such an analysis (which the Examiner does not concede), Applicant also has failed to provide any reasoning other than that the decision "is particularly compelling" (p.2, Remarks) as to why the Office should be bound by a decision that is *non-precidential*. The fact that this decision is *non-precidential* and, thus, non-binding on the Office, is an important detail that Applicant continues to ignore. Furthermore, Applicant's opinion that

the decision is "particularly compelling" and, thus, should be followed is immaterial to the *facts* provided in the case to support the position that the specification lacks enabling guidance for the full scope of the claims, which, incidentally, Applicant also repeatedly fails to address. The fact that the decision may be compelling or interesting does not resolve the lack of enabling guidance in the instant case for the reasons set forth in the previous Office Action at p.2-8. As a result, this argument regarding *Ex parte Cho*, therefore, again remains unimpressive.

Thirdly, and lastly, the allegation that the Examiner has not met her burden of showing why prevention of the other conditions in the claims is also not enabled is unpersuasive. Please see p.3 of the Office Action dated November 25, 2008, which states that, "For the purposes of consideration under 35 U.S.C. 112, first paragraph, the instant rejection focuses on the particular condition of metabolic syndrome, as recited in present claim 1. However, the reasons stated concerning the burden of enabling the prevention of the prediabetic condition of metabolic syndrome apply also to the myriad of other conditions encompassed by the present claims, but for the obvious difference in the type of disorder." In other words, the rejection was set forth such that the logic provided to conclude a lack of enabling guidance regarding the prevention of metabolic syndrome applied equally to the other disorders recited in the claims. Applicant, however, has not provided any reasoning or evidence to negate the idea that the logic set forth in the rejection regarding a lack of enabling guidance regarding prevention does not apply to the other conditions listed in the instant claims. In other words, Applicant is merely alleging on the record that such reasoning does not apply, but provides no evidence or reasons aside from Counsel's own opinion that such is the case. Statements of this nature are unsupported allegations and are clearly unpersuasive in accordance with the guidance provided at MPEP §2145, which states, "The arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997)".

For these reasons *supra*, and those previously made of record at p.2-8 of the Office Action dated November 25, 2008, rejection of claims 2 and 7-13 remains proper.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2 and 7-18 remain rejected under 35 U.S.C. 103(a) as being unpatentable over De Gasparo et al. (WO 01/76573; 2001) in light of Robl et al. (U.S. Patent Application Publication No. 2002/001334; January 31, 2002), cited to show a fact, in view of Cecil's Textbook of Medicine (2000), Harlan et al. (U.S. Patent Application Publication No. 2001/0006656; July 2001) and Bohm et al. (WO 02/15891; February 2002), each already of record, for the reasons of record set forth at p.9-13 of the previous Office Action dated November 25, 2008, of which said reasons are herein incorporated by reference.

Response to Applicant's Arguments

Applicant again traverses the instant rejection, stating that De Gasparo et al. fail to disclose the

specific combination of telmisartan and atorvastatin anywhere in the reference. Applicant further alleges that De Gasparo et al. lists a number of commercially available sartans, including telmisartan, but fails to disclose this specific compound "as a selected compound in the context of a specific combination, much less with atorvastatin" (p.4, Remarks). In fact, Applicant submits that the only sartan mentioned in the reference in the context of a specific combination is valsartan, which Applicant alleges constitutes a teaching away from the use of telmisartan. Applicant makes the same allegations with regard to atorvastatin, stating that the compound is not mentioned in combination with telmisartan. Applicant submits that the secondary references, i.e., Robl et al., Cecil's Textbook of Medicine, Harlan et al. or Bohm et al., do not provide motivation, reasonable expectation of success, or a teaching or suggestion of all of the claim limitations of the invention. Still further, Applicant submits that neither the primary nor the secondary references teach or suggest telmisartan increases the expression of genes regulated by the PPAR-gamma receptor, which is the reason that telmisartan is a preferred combination partner for atorvastatin in the treatment of, e.g., diabetes.

Applicant's traversal has been fully and carefully considered, but fails to be persuasive.

In response, Applicant's attention is once again directed to p.17-18 of the Office Action dated March 30, 2006, which sets forth the teachings of De Gasparo et al. insofar as the reference expressly teaches the combination of an AT1-receptor antagonist in combination with an HMG-CoA reductase inhibitor (p.1, l.27-29), wherein the AT1-receptor antagonist may be selected from, *inter alia*, telmisartan (p.3, l.22) and the HMG-CoA reductase inhibitor may be selected from, *inter alia*, atorvastatin (p.5, l.9-11). De Gasparo et al. clearly contemplates embodiments of the invention wherein the combination of at least two therapeutic components comprises an AT1-receptor antagonist (of which telmisartan is expressly disclosed as one of several interchangeable AT1-receptor antagonists that may be used in the context of the disclosed invention) or a pharmaceutically acceptable salt thereof, and an HMG-CoA reductase inhibitor (of which atorvastatin is expressly disclosed as one of several interchangeable HMG-

CoA reductase inhibitors that may be used in the context of the disclosed invention) or a pharmaceutically acceptable salt thereof. Please reference p.1, p.3, l.22, and p.5, l.9-11 of De Gasparo et al. This teaching is clear, exact and unequivocally speaks to the contrary of Applicant's traversal that the reference fails to disclose the claimed combination.

Applicant appears to be of the persuasion that the lack of a specific example of the disclosed combination of telmisartan and atorvastatin somehow constitutes a complete lack of teaching of the claimed combination and/or constitutes a teaching away from the claimed combination in view of the fact that other combinations of agents are exemplified. This is not persuasive. A preferred or exemplified embodiment (in this case, compositions using valsartan) does not constitute a teaching away from other embodiments disclosed within the four corners of the reference, including non-preferred embodiments. Applicant is reminded that the disclosure of a reference must be considered as expansively as is reasonably possible to determine the full scope of the disclosure and, as a result, is most certainly not limited to that which is preferred and/or exemplified. Please see MPEP at §2123, which states, "A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill in the art, including non-preferred embodiments…Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or non-preferred embodiments." Thus, the fact that other compounds may be exemplified or preferred does not negate or direct the artisan away from the broader teaching of the reference, which expressly provides for, and, thus, clearly contemplates the use of, a combination of an AT1-receptor antagonist (i.e., telmisartan) with an HMG-CoA reductase inhibitor (i.e., atorvastatin). Moreover, Applicant is reminded that there is no legal requirement that a reference *must exemplify* a particular embodiment in order to constitute a teaching of the same. A reference will constitute a teaching so long as the disclosure clearly describes and enables such an embodiment and, in the present case, such description is clearly found in De Gasparo et al.

Applicant's additional attempt to patentably distinguish the claimed invention over that of the

prior art by asserting that neither the primary nor the secondary references teach or suggest that telmisartan increases the expression of genes regulated by the PPAR-gamma receptor is, as before, not persuasive. The fact that Applicant has recognized another advantage of the combination of telmisartan and atorvastatin, when the prior art already acknowledges the desirability of this same combination for the identical therapeutic objectives as presently claimed, cannot be the basis for patentability. Please see *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

The explanation of an effect obtained when using a compound cannot confer novelty on a known process if the skilled artisan was already aware of the occurrence of the desired therapeutic effect. In the instant case, even if De Gasparo et al., did not recognize the advantageous effect on increasing expression of genes regulated by PPAR-gamma when telmisartan and atorvastatin were combined, the fact that Applicant has recognized this advantage is not considered a new therapeutic application because the known treatment of the same diseases as presently claimed using this combination of active agents was already known and recognized in the prior art. Though mechanisms of action of chemical entities are no doubt important contributions to scientific and pharmaceutical development, the assessment of patentability under 35 U.S.C. 103 is based upon the therapeutic applications and effects of the compounds, not the mechanism by which they exert such a therapeutic effect.

Applicant again states that "none of Robl et al., Cecil's Textbook of Medicine, Harlan et al., or Bohm et al. provide what De Gasparo et al. lacks in providing to one of skill in the art as a motivation, reasonable expectation of success, or teaching or suggestion of all of the claim limitations of the claimed invention" (p.4, Remarks), which is also, as before, not persuasive. The record clearly indicates that one of ordinary skill in the art would have been motivated to combine the cited references in such a manner to render the presently claimed invention *prima facie* obvious with a reasonable expectation of success in making such a combination, absent factual evidence to the contrary, and Applicant has failed to provide any factual evidence to the contrary. Applicant's attention is directed to p.16-22 of the rejection presented

in the previous Office Action dated March 31, 2006 for this reasoning, which will not be repeated herein so as not to burden the record.

Additionally, Applicant is again reminded that rejections made under 35 U.S.C. 103(a) are based upon the combination of references. As a result, focusing solely on the discrete teachings of each of the cited references is tantamount to examining each of them inside of a vacuum and fails to be persuasive in establishing non-obviousness because it is the *combined* teachings that are the basis for a proper conclusion of obviousness, not each individual reference alone. In other words, it must be remembered that the references are relied upon in combination and are not meant to be considered separately. To properly conclude obviousness of an invention *does not require the claimed invention to be expressly suggested in its entirety by any one single reference under 35 U.S.C. 103(a)*. Rather, the test is *what the combined teachings* of the references would have suggested to those of ordinary skill in the art. Please reference *In re Young*, 403 F.2d 754, 159 USPQ 725 (CCPA 1968) and *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

For these reasons *supra*, and those previously made of record at p.9-13 of the Office Action dated November 25, 2008, rejection of claims 2 and 7-18 remains proper.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 2 and 7-18 remain provisionally rejected under the judicially created doctrine of

obviousness-type double patenting over claims 1 and 8-35 of U.S. Patent Application No. 10/757,015, in view of Harlan et al. (U.S. Patent Application Publication No. 2001/0006656; 2001), each already of record, for the reasons of record set forth at p.13-14 of the previous Office Action dated November 25, 2008, of which said reasons are herein incorporated by reference.

Applicant states that he will file a Terminal Disclaimer if (1) the instant claims be found otherwise allowable and (2) the copending claims pose a double patenting issue at that time. Applicant states that, since the scope of the claims may change and moot these rejections, there is no need to address these issues at this time.

Insofar as the instant claims are not presently in condition for allowance due to the issues described *infra*, and further that the instant claims and the copending claims raise an issue under the judicially created doctrine of obviousness-type double patenting for the reasons previously set forth in the Office Action dated November 25, 2008 at p.13-14, the rejection is **maintained**.

Claims 2, 7-11 and 14-18 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-10, 12-15 and 18-25 of U.S. Patent Application No. 10/899,784, already of record, for the reasons of record set forth at p.14 of the previous Office Action dated November 25, 2008, of which said reasons are herein incorporated by reference.

Applicant states that he will file a Terminal Disclaimer if (1) the instant claims be found otherwise allowable and (2) the copending claims pose a double patenting issue at that time. Applicant states that, since the scope of the claims may change and moot these rejections, there is no need to address these issues at this time.

Insofar as the instant claims are not presently in condition for allowance due to the issues described *infra*, and further that the instant claims and the copending claims raise an issue under the

judicially created doctrine of obviousness-type double patenting for the reasons previously set forth in the Office Action dated November 25, 2008 at p.14, the rejection is **maintained**.

Claims 2, 7 and 12-18 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-21 of U.S. Patent Application No. 11/300,497 in view of Drug Facts and Comparisons (1996), each already of record, for the reasons of record set forth at p.14-15 of the previous Office Action dated November 25, 2008, of which said reasons are herein incorporated by reference.

Applicant states that he will file a Terminal Disclaimer if (1) the instant claims be found otherwise allowable and (2) the copending claims pose a double patenting issue at that time. Applicant states that, since the scope of the claims may change and moot these rejections, there is no need to address these issues at this time.

Insofar as the instant claims are not presently in condition for allowance due to the issues described *infra*, and further that the instant claims and the copending claims raise an issue under the judicially created doctrine of obviousness-type double patenting for the reasons previously set forth in the Office Action dated November 25, 2008 at p.14-15, the rejection is **maintained**.

Conclusion

Rejection of claims 2 and 7-18 remains proper.

No claims of the present application are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the

mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LESLIE A. ROYDS whose telephone number is (571)-272-6096. The examiner can normally be reached on Monday-Friday (9:00 AM-5:30 PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571)-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leslie A. Royds/
Patent Examiner, Art Unit 1614

June 1, 2009

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614